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KLARQUIST SPARKMAN CAMPBELL
LEIGH & WHINSTON, LLP
One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, OR 97204

EXAMINER
KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
1652	16

DATE MAILED: 07/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/866,570	CROTEAU ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- Th MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6,8,10,11,14 and 24-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3-6* is/are allowed.

6)☒ Claim(s) *8,10,11,14,24,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (Paper No. 13, mailed on January 23, 2003), Applicants filed an amendment and response received on April 25, 2003 (Paper No. 14). Said amendment amended the specification, drawings, and sequence listing, cancelled Claims 1, 9, 16, 18, 23, and 25, and amended Claims 3, 4, 8, 14, and 24. Thus, Claims 3-6, 8, 10-11, 14, and 24-27 are pending in the instant Office action.

Election

2. Previously, Claims 24-27 were not examined because they were not drawn to elected subject matter. Applicants elected a polynucleotide Group relating to SEQ ID NOs: 44/45. Claims 24-27 related to proteins of SEQ ID NOs: 26, 28, 50, 52, 54, 56, and 58 (see Claims 23), NOT SEQ ID NO:45. Thus, Claims 24-27 were properly not examined previously. However, with Applicants' amendment filed April 25, 2003 (Paper No. 14), Claims 24-27 are now drawn to elected subject matter and will be examined herein.

Claims 3-6, 8, 10-11, 14, and 24-27 are pending in the instant Office action and will be examined herein.

Priority

3. As previously noted, the instant application is granted the benefit of priority for the U.S. non-Provisional Application No. 09/457,046 (DIV) filed on December 7, 1999 and 09/411,145 (CIP) filed on September 30, 1999. Moreover, the elected Group drawn to TAX6 does not have priority back to the earliest date of September 30, 1999 since 09/411,145 teaches only TAX1 and TAX2.

Drawings

4. Applicants filed substitute drawings of Figures 4 and 6 on April 25, 2003; said drawings have been entered. To be considered by the Draftsman, a complete set of formal drawings for consideration must be filed in response to the instant Office action and may not be held in abeyance (see 37 C.F.R. § 1.85(a)).

Compliance with the Sequence Rules

5. In response to the previous request to comply with the sequence rules, Applicants amended the sequence listing, the drawings, and the specification to identify all sequence disclosures by SEQ ID NOs. The sequence listing filed on April 25, 2003 has been entered. The instant application now fully complies with the sequence rules.

Withdrawn - Objections to the Specification

6. Previous objection to the specification for being confusing with respect to the sequence listing is withdrawn by virtue of Applicant's amendment to the specification.

7. Previous objection to the specification for updated lacking continuity data in the first paragraph is withdrawn by virtue of Applicants' amendment.

8. Previous objection to the specification because the title is not descriptive is withdrawn by virtue of Applicant's amendment to the title.

9. Previous objection to the specification for inappropriate notation of an internet address is withdrawn by virtue of Applicants' amendment.

10. Previous objection to the specification for having confusing characters throughout the specification is withdrawn by virtue of Applicants' amendment.

Maintained – Objections to the Specification

11. Previous objection to the Abstract for not completely describing the disclosed subject matter is maintained. Applicants' arguments and amendments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue that the claimed subject matter need not be described in the Abstract; however, the Examiner requested no such amendment. The Examiner requested that the Abstract be amended to completed described the ***disclosed*** subject matter, including "the full name of the enzymes disclosed in the specification and the source species, *Taxus cuspidata*, for completeness." Applicants' amendment to the Abstract is insufficient to obviate the objection. An amendment to obviate this objection must include all the enzyme names, not just that which is claimed since the Abstract describes the entire disclosure and not just the claimed invention, as well as the name of the source species. Correction is required.

12. Previous objection to the specification for being confusing in its varied use of the enzyme name for the claimed nucleic acid molecule encoding the TAX6 enzyme is maintained. Applicants' arguments and amendments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue that the specification defines acyltransferase and transacylase as synonyms; this was previously noted by the Examiner (see item c below) and accepted. However, the concern pointed out by the Examiner is with the use of **acyl**transacylase and the more specific O-acetyl transferase. The Examiner pointed out

specific occurrences in the specification where TAX6 was specifically being described – occasions where the specific O-acetyl transferase OR the generic acyltransferase/transacylase should be used consistently (i.e., use the generic or the specific terminology, but do not interchange) to avoid confusion.

a) On page 7, the term "acyltransferase" (as amended) is used to describe TAX6.
b) On page 10, the term "O-acetyl transferase" is used.
c) On page 15, the terms "acyltransferase" and "transacylase" are noted as interchangeable; there is no mention of acetyl transferases in this paragraph.
d) On page 21, the term "O-acetyl transferase" is used.
e) On page 33, line 9, the term "transacylase" is used.
f) On page 35, the term "O-acetyl transferase" is used.

The Examiner understands acyltransferases to transfer and more generic, acyl group while acetyltransferase to specifically transfer an acetyl group. TAX6 should have a consistent enzyme name, whether that be an acyltransferase/transacylase OR an O-acetyl transferase; it is precisely the flip-flop back and forth between these terms that is confusing as to the character of TAX6. The Examiner suggests amending all recitations specific to TAX6 to the term ---O-acetyl transferase--- for clarity. Correction is required.

Withdrawn - Claim Objections

13. Previous objection to Claims 3-6 for depending from a non-elected claim is withdrawn by virtue of Applicants' amendment to Claim 3.

14. Previous objection to Claim 16 for depending from a cancelled claim is withdrawn by virtue of Applicants' cancellation of Claim 16.

15. Previous objection to Claims 3-6, 8, 10, 11, and 14 for containing non-elected subject matter is withdrawn by virtue of Applicants' amendment to the claims.

New Claim Objections

16. Claim 24 is objected to for having improper punctuation. In line 6, the period should be a semi-colon.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

17. Previous rejection of Claim 16 under 35 U.S.C. § 112, second paragraph, as being indefinite for the activity of a transacylase is withdrawn by virtue of Applicant's cancellation of said claim.

18. Previous rejection of Claims 8, 10, 11, and 14 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicants' amendment limiting the scope of the nucleic acid molecules claimed.

New or Maintained - Claim Rejections - 35 U.S.C. § 112

19. Previous rejection of Claims 8, 10, 11, 14, 24, and 26-27 under 35 U.S.C. § 112, second paragraph, as being indefinite for the activity of a transacylase is maintained; new rejection of Claims 24 and 26-27 is added to the instant rejection. Thus, Claims 8, 10, 11, 14, 24, and 26-27 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the activity of a transacylase. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue that the meaning of the term "transacylase" is clear. The Examiner does not dispute the clarity of the broad term, "transacylase" or "acyltransferase".

This instant rejection is based on the fact that "TAX6 that seems to be defined as an acetyltransferase" as previously noted. Thus, it is confusing why the claimed nucleic acid molecule can encode a generic "transacylase" while TAX6 is specifically defined as an O-acetyl transferase. Clarification is required.

20. Claims 24 and 26-27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "conservative amino acid substitutions" is unclear as to its scope. On page 39, a Table of substitutions is described; however, in the text following said Table, "less conservative" mutations are also described. Thus, it is unclear if the term "conservative amino acid substitutions" is limited to only those described in the Table or can they be some broader genus. Clarification is required.

21. Previous rejection of Claims 8, 10, 11, and 14 under 35 U.S.C. § 112, first paragraph, written description, is maintained; new rejection of Claims 24 and 26-27 is added to the instant rejection. Thus, Claims 8, 10, 11, 14, 24, and 26-27 stand rejected under 35 U.S.C. § 112, first paragraph, written description. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that the functional language added to the instant claims obviates the instant rejection. This is not the case. Firstly, the activity cited is unclear – see rejection under 35 U.S.C. § 112, second paragraph, above. Secondly, the activity is not specific. TAX6 is described as a 10-deacetylbaccatin III-10-O-acetyl transferase. The instant specification describes a genus of nucleic acid molecules specifically related to the TAX6 sequence AND having the specific activity described for TAX6. The instant specification does

not describe a genus of nucleic acid molecules specifically related to the TAX6 sequence without having the specific activity described for TAX6.

Withdrawn - Claim Rejections - 35 U.S.C. § 102

22. Previous rejection of Claim 8 under 35 U.S.C. § 102(b) as being anticipated by GenBank Accession Number X66785 is withdrawn by virtue of Applicant's amendment.

Withdrawn - Claim Rejections - 35 U.S.C. § 103

23. Previous rejection of Claims 8, 10, 11, and 14 under 35 U.S.C. § 103(a) as being unpatentable over Menhard *et al.* or Zocher *et al.*, either in view of GenBank Accession Number AF456342, Matsudaira, Wozney, and Sambrook *et al.* is withdrawn by virtue of Applicant's amendment and/or Applicants' arguments and the Examiner's reconsideration. All the instant claims are drawn to nucleic acid molecules having particular sequence identity limitations related to the DNA sequence (SEQ ID NO:44); even in Claim 8, the limitation of "very high stringency" is limited to at least 90% identical in the specification. While isolated O-acetyltransferase proteins are taught from *Taxus chinensis* and *Taxus baccata*, no DNA sequence information is disclosed. Thus, the sequence of the DNA cannot be obviated due to the degeneracy of the genetic code. However, Claims 24 and 26-27 are drawn to nucleic acid molecules encoding a particular protein, which protein has been purified. Thus, a new rejection is set forth against these claims below.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. Claims 24 and 26-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Menhard *et al.* (see IDS) or Zocher *et al.* (see IDS), either in view of GenBank Accession Number AF456342, Matsudaira, Wozney, and Sambrook *et al.* The instant claims are drawn to nucleic acid molecules that encode a protein related to SEQ ID NO:45, which is disclosed as a 10-deacetylbaccatin III-10-O-acetyl transferase.

Menhard *et al.* teach a purified protein from *Taxus chinensis* that performs an acetyltransferase reaction on 10-desacetylbaccatin III (see Abstract).

Zocher *et al.* teach an isolated protein from *Taxus baccata* that acetylates 10-deacetylbaccatin-III (see Abstract).

Neither Menhard *et al.* nor Zocher *et al.* teach the protein sequence or encoding DNA sequence of their acetyltransferases from *T. chinensis* and *T. baccata*, respectively. The natural relatedness of sequence from *Taxus* species of *cuspidata*, *chinensis* and *baccata* is very high as seen in the previously attached alignment of the *cuspidata* (SEQ ID NO:44) and *baccata* (GenBank Accession Number AF456342) sequences (the *baccata* sequence was made available after the priority date of the instant claims and cannot be used as anticipatory art, but is used herein as post-filing date evidence allowed by M.P.E.P. § 2131.01). Moreover, the reactions catalyzed by the isolated proteins of Menhard *et al.* and Zocher *et al.* are identical to the reaction

described for TAX6 in the instant application. And lastly, the protein sequences of the Menhard *et al.* and Zocher *et al.* acetyltransferases are inherent properties of the disclosed proteins.

The skill of an artisan in the field of molecular biology at the time the invention was made was such that the artisan could use conventional techniques to: 1) obtain a partial amino acid sequence of an isolated polypeptide; 2) synthesize a degenerate polynucleotide probe based on the partial amino acid sequence; 3) use the polynucleotide probe to screen a cDNA or genomic library and identify a full length cDNA or genomic clone; 4) construct expression vectors comprising the isolated cDNA or genomic clone; and 5) transform a host cell with an expression vector comprising the isolated cDNA or genomic clone. Specifically, Matsudaira teaches methods for the determination of N-terminal amino acid sequences (see pages 602-604), and Wozney teaches methods of using purified proteins to clone the corresponding genes (see page 738). Wozney teaches the considerations for the selection of peptide candidates for the production of degenerate oligonucleotide probes, synthesis of oligonucleotide probes, screening of genomic or cDNA libraries, and isolation and amplification of cDNA or genomic clones. (see pages 738-751). The teachings of the Matsudaira and Wozney teach methods that enable the skilled artisan at the time the invention was made to produce the DNA that encode the isolated acetyltransferases as taught by either Menhard *et al.* or Zocher *et al.* Thus, the teachings of the isolated or purified acetyltransferases by either Menhard *et al.* or Zocher *et al.* render the DNA encoding said acetyltransferases obvious, because the prior art teachings suggest all the elements of said DNA, and the prior art teachings enabled the artisan to produce said DNA claimed.

Sambrook *et al.* teach vectors, promoters and DNA sequences required for the transcription of cloned copies of genes, generally, and the translation of their mRNAs in

Escherichia coli (see pages 404-411) and eukaryotic cells (see pages 412-433). Sambrook *et al.* also teach methods of maximizing the expression of cloned genes in transformed host cells (see page 431). The teachings of the Sambrook *et al.*, in light of the above teachings of Matsudaira and Wozney, teach methods that enable the skilled artisan at the time the invention was made to produce acetyltransferase-encoding DNA fragments from *Taxus* species in plasmids for recombinant expression of acetyltransferases. Thus, the teaching of the isolated acetyltransferase by either Menhard *et al.* or Zocher *et al.* renders the DNA encoding acetyltransferases and their use in the recombinant expression of acetyltransferases obvious, because the prior art teachings suggest all the elements of the DNA fragments and their use, and the prior art teachings enabled the artisan to produce the DNA fragments and recombinantly express them.

At the time the invention, one of ordinary skill in the art would have been motivated to combine the teachings of Menhard *et al.* or Zocher *et al.* with supporting references Matsudaira, Wozney, Sambrook *et al.* to formulate methods of recombinant expression of the characterized acetyltransferase for the purpose of producing large quantities of the acetyltransferase for further study. One would have been motivated to such studies because of the crucial role this acetyltransferase plays in the biosynthesis of Taxol, a potent and successful anticancer drug (see Menhard *et al.*).

The Examiner notes that due to the inherent sequence of a purified protein, neither Menhard *et al.* nor Zocher *et al.* need disclose the protein sequence to render ***any*** DNA encoding said sequence obvious as described above. The instant rejection does not apply to Claim 3 because neither Menhard *et al.* nor Zocher *et al.* teach the purification of the *Taxus cuspidata*

protein, but only highly related proteins within the limitations of 90% identity and/or conservative substitutions (considering the unclear definition).

Summary of Pending Issues

25. The following is a summary of the issues pending in the instant application:

a) A complete set for formal drawings must be filed for consideration by the Draftsman.

b) The Abstract stands objected to for not completely describing the disclosed subject matter.

c) The specification stands objected to for being confusing in its varied use of the enzyme name for the claimed nucleic acid molecule encoding the TAX6 enzyme.

d) Claim 24 stands objected to for having improper punctuation.

e) Claims 8, 10, 11, 14, 24, and 26-27 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the activity of a transacylase.

f) Claims 24 and 26-27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "conservative amino acid substitutions".

g) Claims 8, 10, 11, 14, 24, and 26-27 stand rejected under 35 U.S.C. § 112, first paragraph, written description.

h) Claims 24 and 26-27 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Menhard *et al.* (see IDS) or Zocher *et al.* (see IDS), either in view of GenBank Accession Number AF456342, Matsudaira, Wozney, and Sambrook *et al.*

Conclusion

26. Claims 3-6 are allowed; Claims 8, 10, 11, 14, 24, and 26-27 are rejected for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

KMK
July 6, 2003